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EXAMINER	
SKELDING, ZACHARY S	
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1644	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/642,642	ZIPORI ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2008 and 02 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *4,8-12,16 and 18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,13-15,17 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks filed December 2, 2008 are acknowledged.

   Claims 1, 6 and 13-17 have been amended.

   Claim 27 has been added.

   Claims 1-27 are pending.

   Claims 4, 8-12, 16 and 18-26 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species of invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 11, 2007.

   Claims 1-3, 5-7, 13-15, 17 and 27 are under examination as they read on polynucleotides comprising a transcript of a T cell receptor (TCR) gene, said polynucleotide transcript lacking V region sequences and comprising: a constant (C) domain; a joining (J) region sequence; and a 5' intronic J sequence that is upstream to said J region sequence, wherein said 5' intronic J sequence includes an in-frame methionine codon, wherein the species of C domain, J region and 5' intronic J sequences are "Jβ", and the particular species of intronic Jβ sequences are the intronic Jβ sequences upstream of Jβ2.3 and Jβ2.6 which encode the polypeptides of SEQ ID NOs: 17 and 2, respectively.

2. This Office Action is in response to applicant's remarks and amendments filed April 30, 2008 and December 2, 2008.

   The previous grounds of rejection can be found in the Office Action mailed January 2, 2008.

   The prior rejection under 35 U.S.C. § 112, 2nd paragraph has been withdrawn upon further consideration and in view of applicant's amendments to the claims.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

   > The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 5-7 and 13-15 are rejected, and newly presented claim 27 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated polynucleotides encoding the polypeptides of SEQ ID NOs: 37, 39 or 2, such as SEQ ID NO: 38 which encodes SEQ ID NO: 39, does not reasonably provide

enablement for any isolated polynucleotide wherein said isolated polynucleotide comprises a transcript of a T cell receptor (TCR) gene, the polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, essentially for the reasons of record as put forth in the Office Action mailed December 2, 2008.

The disclosure of the specification does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states on page 1404, "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

Applicant argues the claimed polynucleotides are enabled because the skilled artisan could screen mesenchymal stem cells for the expression of the claimed polynucleotides via PCR because "PCR screening is a simple, relatively low cost, extremely sensitive and ultra-rapid procedure and well known to one skilled in the art. For example, a skilled artisan who wishes to analyze a TCR type in a mesenchymal tissue or cell can simply use PCR screening." Moreover, applicant continues, "[t]he use of PCR screening is exemplified in Examples 2, 3 and 5 of the published patent application." (See applicant's remarks filed December 2, 2008, page 10, 2nd paragraph).

Applicant's arguments have been considered, but have not been found convincing, essentially for the reasons of record as put forth in the Office Action mailed January 2, 2008.

The examiner is in agreement with applicant that practicing PCR is well established in the art. However, the issue is not can the skilled artisan perform a PCR reaction, but what sort of experimentation would be required to use the PCR reaction to determine if any given polynucleotide of the invention can be used for either modulating mesenchymal cell growth or detecting mesenchymal cells that can be used in would healing?

It is the examiner's position that far more than routine experimentation would be required of the skilled artisan to determine which particular transcripts, if any, are useful in this regard.

The reason for this is because "Mesenchymal cells" are a phenotypically heterogeneous population of cells including, for example, cells with pluripotency such as mesenchymal stem cells and fibroblast-like mesenchymal cells, as well as more highly differentiated cells such as endothelial-like mesenchymal cells, adipocytic mesenchymal cells and osteoblastic mesenchymal cells (see, for example, Benayahu et al., Calcif Tissue Int. 1991 Sep;49(3):202-7, in particular page 202). Moreover, these different types of mesenchymal cells have phenotypically diverse expression of many different markers, e.g., alkaline phosphatase (see, Benayahu et al., ibid, in particular page 204, right column, 3rd paragraph) and extracellular matrix protein (see, Zipori et al., Blood. 1985 Aug;66(2):447-55, in particular page 449, Table 1).

Given the variety of mesenchymal cells and their functional differences, the skilled artisan would not be able to reliably predict, which, if any polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon, other than SEQ ID NO: 38, would be useful for either modulating mesenchymal cell growth or detecting mesenchymal cells that can be used in would healing, and undue experimentation would be required to determine which particular transcripts, if any, are useful in this regard.

With respect to applicant's assertions concerning the lack of Jint-Jβ2.1-Cβ2 mRNA expression in the MBA-13 cell strain as shown in post-filing date art as compared to the teachings of the instant specification, applicant's assertions are acknowledged but they do not overcome the outstanding grounds of rejection as to this particular embodiment of applicant's invention.

While applicant's assertion that "[t]he plasticity of stem cells and mesenchymal cells is well known," and "[s]uch plastic nature may account for variability in the behavior of cultured cells," is indeed supported by objective evidence of record (see, e.g., Applicant's Appendix 2 submitted April 30, 2008, Dov Zipori, Curr Stem Cell Res Ther. 2006 Jan;1(1):95-102, in particular page 97, right column, 1st paragraph to end, including Figures 4-6 in particular), this only serves to emphasize the unpredictability of gene expression that would be expected in mesenchymal cells as compared to cells with less "plasticity", be they committed progenitor stem cells or fully differentiated somatic cells.

Given the plasticity and variability of gene expression in mesenchymal stem cells, far more than routine experimentation would be required to determine if any polynucleotide lacking V region sequences and comprising a constant (C) domain and

joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon, other than SEQ ID NO: 38, would be useful for either modulating mesenchymal cell growth or detecting mesenchymal cells.

Applicant further asserts that while MSC are plastic and exhibit variability in their behavior, "[t]his, however, does not mean that primary cells isolated from the animal or human, when examined shortly thereafter, would be variable. To the contrary, such cells are relatively uniform. Indeed, most mesenchymal isolates, at first passages, are similar and one can, with great certainty, say that any normal mouse strain or a human individual will harbor TCR in the mesenchyme. This is certainly the case for fresh tissues." (see applicant's remarks filed December 2, 2008, paragraph bridging pages 9-10).

Based on this assertion, applicant appears to be arguing that the claimed polynucleotides are enabled.

However, applicant's argument is not found convincing for multiple reasons.

First, it is unclear exactly what applicant is arguing. For example, does "To the contrary, such cells are relatively uniform. Indeed, most mesenchymal isolates, at first passages, are similar and one can, with great certainty, say that any normal mouse strain or a human individual will harbor TCR in the mesenchyme" mean the skilled artisan can say "the mesenchyme" from any normal mouse strain or a human individual will harbor T cells which will be present in the mesenchymal isolate, or is applicant making an assertion about mesenchymal stem cells expressing the claimed polynucleotide?

Secondly, applicant has provided no sound scientific reasoning or objective evidence in support of their assertions regarding "TCR in the mesenchyme" and arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). See MPEP § 2145.

Applicant further asserts "With respect to the Carroll reference (Cell, 2000, 101 (6): 577-580), Applicants note that this reference fails to describe or suggest T cell receptors, in contrast to the claimed invention. Instead, the Carroll reference discusses the evolution of morphological diversity and, more specifically, the importance of cis-regulatory DNA and transcription factors in this phenomenon. Functional diversity or diversity at the protein level are not addressed. Moreover, there is nothing in the Carroll reference that suggests that similar genes do not share a similar function across species." (see applicant's remarks filed December 2, 2008, paragraph bridging page 10, 2nd paragraph).

It is the examiner's position the Carroll reference provides sound scientific support for the notion that even if the skilled artisan knows a polynucleotide such SEQ ID NO: 38, which encodes SEQ ID NO: 39, is useful for detecting mouse embryonic fibroblasts which are useful, for example, in wound healing, the instant specification does not sufficiently enable the skilled artisan to extrapolate from this knowledge to using any isolated polynucleotide encompassed by claim 1, such as human polynucleotides encompassed by claim 1, commensurate in scope with the claimed invention with any measure of predictability.

Note in this regard the instant specification does not teach how to use the breadth of the claimed polynucleotides to modulate mesenchymal cell growth or detect mesenchymal cells that can be used in would healing.

Rather, as stated in the previous Office Action, the instant specification discloses that PCR analysis detected the Jint-Jβ2.1-Cβ2 mRNA in the tumorogenic mesenchymal cell line MBA-13; however as described in the previous Office Action, a post-filing date publication contradicts the disclosure of the instant specification in that it shows mRNA analysis of the mesenchymal cell line MBA-13 does not detect Jint-Jβ2.1-Cβ2 (see Barda-Saad et al., Oncogene. 2002 Mar 27;21(13):2029-36, in particular, page 2032 Figure 2E, cited on IDS of January 21, 2005).

Thus, the skilled artisan would not know how to use Jint-Jβ2.1-Cβ2, without undertaking undue experimentation, to modulate mesenchymal cell growth or as a "diagnostic marker" for the detection of a mesenchymal cells that can be used in would healing for example, such as mouse embryonic fibroblasts.

Moreover, simply showing that a polynucleotide transcript of a T cell receptor (TCR) gene encompassed by the instant claims can be isolated from human cord blood mononuclear cells and human amniotic fluid cells, as is the case with SEQ ID NO: 67, does not provide sufficient direction or guidance for the skilled artisan to use SEQ ID NO: 67 as taught in the instant specification.

For example, before using SEQ ID NO: 67 or the polypeptide encoded thereby to modulate mesenchymal cell growth or to detect of mesenchymal cells that can be used in would healing, for example, mouse embryonic fibroblasts, the skilled artisan would first have to determine, at a minimum, which, if any mesenchymal cells express SEQ ID NO: 67, and this is not a matter of routine experimentation as described above.

In conclusion, the instant claims encompass an invention of tremendous breadth, and essentially call for trial and error by the skilled artisan to begin discovering how to use the claimed invention without assisting the skilled artisan in such an endeavor, which is insufficient to constitute adequate enablement.

As put forth in Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005), "[i]f mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

Similarly, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc, v. Novo Nordisk, 42 USPQ 2d 1001,(CAFC 1997), the court held: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". Further, "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not found enabling for the breadth of the claimed invention because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 2, 6, 7, 13 and 14 are rejected, and new claim 27 is rejected, under 35 U.S.C. 102(e) as anticipated by Olga Bandman (US 20020137081) as evidenced by Entrez Nucleotide accession number L34740 (http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=nuccore&id=1100190), Entrez Protein accession number AAA82687 (http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=protein&id=1100191), and IGc domain description (http://www.ncbi.nlm.nih.gov/Structure/cdd/cddsrv.cgi?uid=28981), essentially for the reasons of record put forth in the Office Action mailed January 2, 2008.

Applicant argues Bandman does not anticipate the instant claims because:

- The Bandman sequence does not even contain the entire exon 4 [of the Cβ2 domain], since the last nucleotide aligns with base 204439 of U66061 (enclosed as Appendix 4), which is 12 nucleotides before the end of exon 4 of the Cβ2 domain, situated at base 204451. Moreover, the Bandman sequence even seems to lack the poly A signal, situated between bases 204446-204451 of U66061 (see Appendix 4).

- Furthermore, a translation map of the Bandman sequence and its nucleotide assignment, as shown in Appendix 5, shows that the Bandman sequence comprises two different JB2 sequences (JB2.3 and JB2.4) that are separated by an intron sequence. It also shows the presence of multiple stop codons, as mentioned above and underlined in Appendix 5, the first of which is placed at the start of the C region sequence. The presence of the stop codon at this particular position in the Bandman sequence would cause the sequence to be untranslatable. Moreover, there is no indication in the Bandman application that SEQ ID NO: 130 was successfully expressed in an expression system or transfected into a mammalian cell host, contrary to the claimed polynucleotide transcript.

- In addition, the present application recites "... a transcript of a TCR gene...lacking V region sequences and comprising a C domain and joining (J) region sequences and a 5' intronic J sequences upstream...including an in-frame methionine codon." The Bandman sequence has multiple J sequences separated by an intron. This is not equivalent to the claimed polynucleotide transcript or to its expressed protein.

- Claim 27 specifically recites the mesenchymal (stromal) origin of the TCR transcript. This further distinguishes the invention from Bandman, which describes a plurality of cDNAs expressed in vascular tissue and their use for diagnosis, monitoring and treatment of vascular disorders.

Applicant's arguments have been considered, but have not been found convincing, essentially for the reasons of record as put forth in the Office Action mailed January 2, 2008 and as explained forth further below.

As to applicant's first argument that the Bandman sequence does not contain the entire exon 4 of Cβ2, this is indeed true as demonstrated by applicant's alignment in Appendix 4 of their Remarks field December 2, 2008.

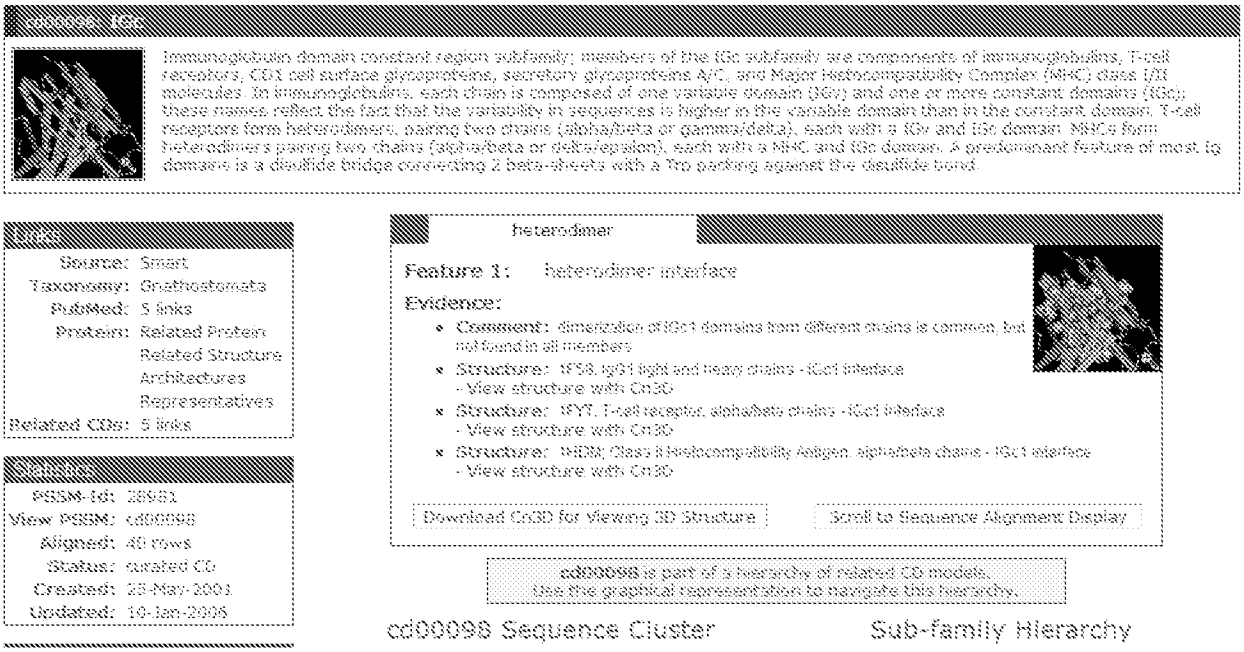
However, insofar as applicant is making the argument that this distinguishes the claimed invention from Bandman, this is not found convincing because it is not a claimed limitation that the isolated polynucleotide transcript comprise full length Cβ2. Rather, the instant claims, recite "an isolated polynucleotide comprising a transcript of a T cell receptor (TCR) gene, said transcript lacking V region sequences and comprising: a constant (C) domain;…"

As put forth in the previous Office Action, "SEQ ID NO: 130 of Bandman further comprises nucleotides 325-730 which are identical but for 2 mismatches to nucleotides 1-406 of the polynucleotide sequence of the human TCR β chain constant (C) domain shown, for example, in Entrez Nucleotide accession number L34740, where SEQ ID NO: 130 of Bandman is the Sbjct and Entrez Nucleotide accession number L34740 is the Query (alignment prepared using the BLAST two sequences program publicly available at http://www.ncbi.nlm.nih.gov/blast/ bl2seq/wblast2.cgi):

```
 Score =  769 bits (400),  Expect = 0.0
 Identities = 404/406 (99%), Gaps = 0/406 (0%)
 Strand=Plus/Plus

Query  1    GAGGACCTGAAAAACGTGTTCCCACCCGAGGTCGCTGTGTTTGAGCCATCAGAAGCAGAG  60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  325  GAGGACCTGAAAAACGTGTTCCCACCCGAGGTCGCTGTGTTTGAGCCATCAGAAGCAGAG  384

Query  61   ATCTCCCACACCCAAAAGGCCACACTGGTATGCCTGGCCACAGGCTTCTACCCCGACCAC  120
            |||||||||||||||||||||||||| ||||||||||||||||||||||||||||||||
Sbjct  385  ATCTCCCACACCCAAAAGGCCACACTGGTGTGCCTGGCCACAGGCTTCTACCCCGACCAC  444

Query  121  GTGGAGCTGAGCTGGTGGGTGAATGGGAAGGAGGTGCACAGTGGGGTCAGCACAGACCCG  180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  445  GTGGAGCTGAGCTGGTGGGTGAATGGGAAGGAGGTGCACAGTGGGGTCAGCACAGACCCG  504

Query  181  CAGCCCCTCAAGGAGCAGCCCGCCCTCAATGACTCCAGATACTGCCTGAGCAGCCGCCTG  240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  505  CAGCCCCTCAAGGAGCAGCCCGCCCTCAATGACTCCAGATACTGCCTGAGCAGCCGCCTG  564

Query  241  AGGGTCTCGGCCACCTTCTGGCAGAACCCCCGCAACCACTTCCGCTGTCAAGTCCAGTTC  300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  565  AGGGTCTCGGCCACCTTCTGGCAGAACCCCCGCAACCACTTCCGCTGTCAAGTCCAGTTC  624

Query  301  TACGGGCTCTCGGAGAATGACGAGTGGACCCAGGATAGGGCCAAACCCGTCACCCAGATC  360
            |||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Sbjct  625  TACGGGCTCTCGGAGAATGACGAGTGGACCCAGGATAGGGCCAAACCTGTCACCCAGATC  684

Query  361  GTCAGCGCCGAGGCCTGGGGTAGAGCAGACTGTGGCTTCACCTCCG  406
            |||||||||||||||||||||||||||||||||||||||||||||
Sbjct  685  GTCAGCGCCGAGGCCTGGGGTAGAGCAGACTGTGGCTTCACCTCCG  730
```

Furthermore, residues 325-730 of Bandman SEQ ID NO: 130 encode a polypeptide identical to the human TCR β chain constant (C) domain, in particular residues 1-135 of a human TCR β chain constant (C) domain shown, for example, in Entrez Protein accession number AAA82687 (note that the polypeptide of AAA82687 is encoded by Entrez Nucleotide accession number L34740 cited above).

As can be seen from the Entrez Protein accession number AAA82687, residues 6 to 108 AAA82687 correspond to the "IGc domain" of the human TCR β chain constant (C) domain which forms the heterodimer interface between the TCR β and α subunits:



(See http://www.ncbi.nlm.nih.gov/Structure/cdd/cddsrv.cgi?uid=28981 for additional information about the "IGc domain")."

Thus, SEQ ID NO: 130 of Bandman encodes a "constant (C) domain" as claimed.

As to applicant's second argument, the presence of two different Jβ2 sequences (JB2.3 and JB2.4) in SEQ ID NO: 130 of Bandman and multiple stop codons, the first of which "is placed at the start of the C region sequence" (when considered with reference to the ORF comprising the DNA encoding the Jβ2.3 polypeptide sequence), these assertions are acknowledged, however SEQ ID NO: 130 of Bandman nevertheless anticipates the claimed polynucleotide.

The claimed polynucleotide "comprises...a joining (J) region sequence…," and thus the presence of addition joining (J) region sequences is not precluded from the claimed polynucleotide.

Moreover, the limitation "a 5' intronic J sequence that is upstream to said J region sequence, wherein said 5' intronic J sequence includes an in-frame methionine codon," does not specify what exactly the "in-frame methionine codon" is in-frame with, and as shown by Applicant's Appendix 5, SEQ ID NO: 130 of Bandman does have a 5' intronic J sequence including an in-frame methionine codon.

As to applicant's argument that "…the Bandman sequence…shows the presence of multiple stop codons…the first of which is placed at the start of the C region sequence. The presence of the stop codon at this particular position in the Bandman sequence would cause the sequence to be untranslatable," this argument is not found convincing for the reasons put forth in the preceding paragraph and further because applicant is arguing limitations not claimed.

For example, the claims do not require the claimed polynucleotide be translatable.

Nevertheless, it is worth pointing out that as asserted by applicant on page 12, 2nd paragraph of their Remarks filed December 2, 2008, Bandman SEQ ID NO: 130 does encode a polypeptide (when translated starting from the first in frame methionine codon) identical to the first 46 amino acids of the polypeptide encoded by SEQ ID NO: 67 of the instant application (see Applicant's "Appendix 5" submitted December 2, 2008).

Furthermore, this Bandman polypeptide encoded by SEQ ID NO: 130 continues for an additional 52 amino acids to give a total of 46 + 52 = 98 amino acids (again see Applicant's "Appendix 5" submitted December 2, 2008).

While applicant asserts "[t]he presence of the stop codon at this particular position in the Bandman sequence would cause the sequence to be untranslatable," applicant has provided no sound scientific reasoning or objective evidence that this 97 amino acid polypeptide would not be translated. In this regard it is noted that the arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). See MPEP § 2145.

As to applicant's argument that "there is no indication in the Bandman application that SEQ ID NO: 130 was successfully expressed in an expression system or transfected into a mammalian cell host, contrary to the claimed polynucleotide transcript," Bandman does not have to provide a working example of the successfully expression of SEQ ID NO: 130 or its successful transfected into a mammalian cell host.

Furthermore, a reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

As stated in the previous Office Action, "Bandman…teaches expression of the cDNAs of the invention by cloning into an expression vector and transfection of a mammalian host cells with said cDNA containing expression vector (see, in particular, pages 7-8, paragraphs [0081]-[0085])."

In contrast, applicant has not provided sound scientific reasoning or objective evidence that the skilled artisan would not know how to clone SEQ ID NO: 130 into an expression vector or how to transfect a mammalian cell host with said expression vector.

As to applicant's third argument that "the Bandman sequence has multiple J sequences separated by an intron. This is not equivalent to the claimed polynucleotide transcript or to its expressed protein," as stated above this amounts to arguing limitations not claimed. The claimed polynucleotide is not limited to having one and only one jointing (J) region.

As to applicant's third argument that "Claim 27 specifically recites the mesenchymal (stromal) origin of the TCR transcript. This further distinguishes the invention from Bandman, which describes a plurality of cDNAs expressed in vascular tissue and their use for diagnosis, monitoring and treatment of vascular disorders," applicant is again arguing a limitation not claimed.

New claim 27 recites "the polynucleotide according to claim 1, wherein the transcript is expressed in stromal mesenchymal cells."

However, the polynucleotide of claim 27 is not distinguished over SEQ ID NO: 130 of Bandman because recitation of "wherein the transcript is expressed in stromal mesenchymal cells" does not carry any patentable weight.

The "polynucleotide of claim 1" is still the "polynucleotide of claim 1" whether the transcript it comprises is "expressed in stromal mesenchymal cells," in some other cell, in vitro or not expressed at all.

In this regard it is noted that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). See MPEP § 2112.01.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory

period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding
Patent Examiner, Art Unit 1644
March 15, 2009

/Michail A Belyavskyi/
Primary Examiner, Art Unit 1644